5: Am J Vet Res. 2003 Feb;64(2):216-24. Related Articles, Li

Antagonism of adenosine receptors by caffeine and caffeine metabolites in equine forebrain tissues.

Chou CC, Vickroy TW.

Department of Physiological Sciences, College of Veterinary Medicine, University of Florida, Gainesville, FL 32610-0144, USA.

OBJECTIVE: To determine the presence of adenosine receptor subtypes A1 : A2a in equine forebrain tissues and to characterize the interactions of caffeine and its metabolites with adenosine receptors in the CNS of horses. SAMPLE POPULATION: Brain tissue specimens obtained during necropsy from 5 adu male research horses. PROCEDURE: Membrane-enriched homogenates from cerebral cortex and striatum were evaluated by radioligand binding assays wit the A1-selective ligand [3H]DPCPX and the A2a-selective ligand [3H]ZM241385. Functional responses to adenosine receptor agonists and antagonists were determined by a nucleotide exchange assay using [35S]-guanosine 5'-(gamma-thio) triphosphate ([35S]GTPgammaS). RESUL' Saturable high affinity [3H]DPCPX binding (A1) sites were detected in cereb cortex and striatum, whereas high-affinity [3H]ZM241385 binding (A2a) site were detected only in striatum. Caffeine and related methylxanthines had simi binding affinities at A1 and A2a sites with rank orders of drug binding affiniti (theophylline > paraxanthine > or = caffeine >> theobromine) similar to other species. [35S]GTPgammaS exchange revealed that caffeine and its metabolite act as pure adenosine receptor antagonists at concentrations that correspond A1 and A2a receptor binding affinities. CONCLUSIONS AND CLINICAL RELEVANCE: Results of our study affirm the presence of guanine nucleotid binding protein linked adenosine receptors (ie, high-affinity A1 and A2a adenosine receptors) in equine forebrain tissues and reveal the antagonistic actions by caffeine and several biologically active caffeine metabolites. Antagonism of adenosine actions in the equine CNS by these stimulants may l responsible for some central actions of methylxanthine drugs, including moto stimulation and enhanced racing performance.

PMID: 12602592 [PubMed - indexed for MEDLINE]